Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Grein J, Ohmagari N, Shin D, et al. Compassionate use of remdesivir for patients with severe Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2007016

Table of contents

Site Personnel

NAME	AFFILIATION
Seyed Ghafouri	Mackenzie Health, Richmond Hill, Canada
Pegah Pourgolafshan	Mackenzie Health, Richmond Hill, Canada
Prof. Denis Malvy	Division of Infectious Diseases and Tropical Medicine, University Hospital of Bordeaux, Bordeaux, France
Arnaud Desclaux	Division of Infectious Diseases and Tropical Medicine, University Hospital of Bordeaux, Bordeaux, France
Björn-Erik Ole Jensen	Universitätsklinikum Düsseldorf, Düsseldorf, Germany
Johannes Georg Bode	Universitätsklinikum Düsseldorf, Düsseldorf, Germany
Renato Maserati	Università di Pavia, Pavia, Italy
Alberto Matteelli	ASST Spedali Civili di Brescia, Spedali Civili Hospital, Brescia, Italy
Luisa Marchioni	National Institute for Infectious Diseases, L. Spallanzani, Rome, Italy
Alessandra D'Abramo	National Institute for Infectious Diseases, L. Spallanzani, Rome, Italy
Prof. Paolo Bonfanti	San Gerardo Hospital, ASST Monza, University of Milan-Bicocca, Monza, Italy
Dr. Guglielmo Marco Migliorino	San Gerardo Hospital, ASST Monza, University of Milan-Bicocca, Monza, Italy
Raffaele Bruno	Division of Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
Francesco Mojoli	Anesthesia and Intensive Care, Emergency Department, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
Yasuhiro Norisue	Department of Critical Care Medicine, Tokyo Bay Urayasu Ichikawa Medical Center, Chiba, Japan
Yuri Kunitani	Department of Medical Technology, Tokyo Bay Urayasu Ichikawa Medical Center, Chiba, Japan
Takumi Umemura	Tosei General Hospital, Aichi, Japan
Yutaka Tokue	Gunma University Hospital, Gunma, Japan
Masakiyo Yatomi	Gunma University Hospital, Gunma, Japan
Kunio Yanagisawa	Gunma University Hospital, Gunma, Japan
Kenichiro Yamada	Hiratsuka City Hospital, Hiratsuka, Kanagawa, Japan
Yasushi Kaneko	Hiratsuka City Hospital, Hiratsuka, Kanagawa, Japan
Kayoko Hayakawa, MD	AMR Clinical Reference Center, Diseases Control Center, National Center for Global Health and Medicine, Tokyo, Japan
Luis Gonzalez del Valle	Hospital Universitario La Paz- Carlos III, Madrid, Spain
Juan C Figueira	Hospital Universitario La Paz- Carlos III, Madrid, Spain
Sarkis Arabian, DO	San Bernardino Regional Medical Center
Brett Giroir, MD	United States Public Health Service Commissioned Corps, Washington, DC
Julie Erb-Alvarez	United States Public Health Service Commissioned Corps, Washington, DC
Andrew Levinson, MD	Miriam Hospital, Providence, RI
John Lonks, MD	Miriam Hospital, Providence, RI
Carol A. Kemper, MD	El Camino Hospital, Mountain View, CA
Mena Senecal, PharmD	Providence Regional Medical Center Everett, Everett, WA
R. Eliot Fagley, MD	Virginia Mason Medical Center, Seattle, WA

NAME	AFFILIATION
Ashwin Gopalan, MD	Virginia Mason Medical Center, Seattle, WA
Michelle Nichols, MD	University of Washington Medical Center - Northwest, Seattle, WA
Bijan J. Ghassemieh, MD	University of Washington Medical Center - Northwest, Seattle, WA
Adriano Lazzarin	Department of Infectious diseases, IRCCS, San Raffaele Institute, Milano, Italy
Chiara Oltolini	Department of Infectious diseases, IRCCS, San Raffaele Institute, Milano, Italy
Romina Corsini	Azienda USL-IRCCS Reggio Emilia Italy
Giovanni Dolci	University of Modena Reggio Emilia, Italy
Melony Chakrabarty, MD	UC Davis Health, Sacramento, CA
Minh-Vu Nguyen, MD	UC Davis Health, Sacramento, CA
Wolfgang Hoepler, MD	Kaiser Franz Josef Hospital, Vienna, Austria
Erich Pawelka, MD	Kaiser Franz Josef Hospital, Vienna, Austria
Bhavna Malik, MD	John Muir Health, Walnut Creek, CA

Baseline Assessment Form for Remdesivir Compassionate Use Program

Remdesivir (RDV; GS-5734) for the Treatment of Selected Coronavirus (CoV) Infection
Single Patient Protocol

Clinical Baseline Assessment Form
This form is ONLY to be completed via email if EDC (https://www.imedidata.com) is unavailable at your site and you are prompted to do so by Gilead Clinical Operations. Please provide as much of the information below as possible and submit to remdesivir_CDM@gilead.com

Patient ID

Institution Name:_____

Physician Name: _____

Patient Initials (XXX): __ __ __

Sex at Birth: [ ] Male [ ] Female

Date of Birth (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Pregnant: [ ] Yes [ ] No [ ] Unknown [ ] NA

Breastfeeding: [ ] Yes [ ] No [ ] Unknown [ ] NA

COVID-19 Disease Status

Current date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Currently hospitalized? [ ] Yes [ ] No

Currently in Intensive Care Unit (ICU) or Critical Care Unit (CCU)?? [ ] Yes [ ] No

First hospital admission date for COVID-19 (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

COVID-19 Symptom onset date (DD/MMM/YYYY): __ __ / __ __ __ / __ __ __ __

Was SARS-CoV-2 confirmed by PCR test? [ ] Yes [ ] No

Radiographic evidence of pulmonary infiltrates? [ ] Yes [ ] No

If Yes, please describe:

Current Vital Signs

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Collection Time (00:00 – 23:59): __ __ : __ __			
Max Body Temperature in Last 24 hours	_____	Units: [ ] Celsius [ ] Fahrenheit	Location: [ ] Armpit [ ] Ear [ ] Oral [ ] Rectum
Resting Respiratory Rate (breaths/min)	_____		
Resting Heart Rate (beats/min)	_____		
SBP (mmHg)	_____		

Baseline Assessment Form for Remdesivir Compassionate Use Program (continued)

DBP (mmHg)	_____
Level of Consciousness	[ ] Alert [ ] Arousable only to Voice or Pain [ ] Unresponsive

Clinical Support, Limitations, and Infection Control

Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Collection Time (00:00 – 23:59): __ __ : __ __	
Currently on room air?	[ ] Yes [ ] No If Yes, please enter oxygen saturation (SpO_2, %):_____
Currently requiring low-flow oxygen therapy (via low-flow nasal cannula or prongs, simple face mask, etc)?	[ ] Yes [ ] No If Yes, then indicate supplemental oxygen amount: ____(L / min) or _____% FiO_2 If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring high-flow oxygen (via e.g., high-flow nasal cannula)?	[ ] Yes [ ] No If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring non-invasive positive pressure ventilation (via BIPAP, CPAP, etc)?	[ ] Yes [ ] No If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring mechanical ventilation (via endotracheal tube, tracheostomy tube, etc)?	[ ] Yes [ ] No If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Currently requiring ECMO support?	[ ] Yes [ ] No If Yes, please indicate type: [ ] V-V [ ] V-A If Yes, please enter start date: (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Ongoing medical care preventing hospital discharge (COVID-19 related or other medical condition)?	[ ] Yes [ ] No
Limitations of physical activity (self assessed)?	[ ] Yes [ ] No
Requiring vasopressor or inotropic support?	[ ] Yes [ ] No

Baseline Assessment Form for Remdesivir Compassionate Use Program (continued)

Other information on clinical course, exposure history, current clinical status

Past Medical History

Medical History Condition	Start Date	Stop Date or indicate as Ongoing

Medications taken in last 48 hours

Include other antiviral medications (e.g., lopinavir/ritonavir, interferon, oseltamivir, etc)

Medication Name	Indication	Dose	Route	Start Date	Stop Date or indicate as Ongoing

Most Recent Laboratory Measures[a]

Chemistry Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __
Chemistry Specimen Collection Time (00:00 – 23:59): __ __ : __ __

Lab Name	Result	Units
Alanine aminotransferase (ALT)		
Alkaline Phosphatase		
Aspartate Aminotransferase (AST)		
Bicarbonate		
Blood Urea Nitrogen (BUN)		
Chloride		
Creatinine		
Creatinine Clearance – Cockcroft-Gault[b]		
Creatinine Clearance – eGFR[b]		

Baseline Assessment Form for Remdesivir Compassionate Use Program (continued)

Creatinine Clearance – CKD-EPI[b]		
Potassium		
Sodium		
Total Bilirubin		
Hematology Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Hematology Specimen Collection Time (00:00 – 23:59: __ __ : __ ____ __		
Lab Name	Result	Units
White Blood Cells		
Hemoglobin		
Hematocrit		
Platelets		
Neutrophils		
Lymphocytes		
Eosinophils		
Coagulation Specimen Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ Coagulation Specimen Collection Time (00:00 – 23:59: __ __ : __ __		
Lab Name	Result	Units
Prothrombin Time		
International Normalized Ratio		
Activated Partial Thromboplastin Time		

SARS-CoV-2 PCR Collection Date (DD/MMM/YYYY): __ __ / __ __ __/ __ __ __ __ SARS-CoV-2 PCR Specimen Collection Time (00:00 – 23:59: __ __ : __ __			
Lab Name	Specimen Source (nasopharynx, oropharynx, BAL, sputum, stool, blood)	Result	Units
SARS-CoV-2 PCR - qualitative			
SARS-CoV-2 PCR - quantitative			

[a] Representative template for lab reporting. Can alternatively forward lab report (with personally identifying information removed)

[b] Need enter only one Creatinine Clearance measure

Table S1. Baseline predictors of clinical improvement

Variable	Hazard Ratio (95% CI*)
Age, per year	0.965 (0.943, 0.987)
<50 years	--
50 to <60 years	0.756 (0.297, 1.923)
60 to <70 years	0.590 (0.228, 1.523)
≥70 years	0.289 (0.113, 0.740)
Female sex	0.811 (0.362, 1.815)
Region of enrollment	
United States	--
Japan	0.432 (0.157, 1.189)
Europe/Canada	0.528 (0.239, 1.167)
Oxygen support status	
Noninvasive oxygen support	--
Invasive ventilation	0.333 (0.164, 0.676)
Duration of symptoms prior to remdesivir treatment, per day	0.999 (0.912, 1.095)
Comorbidities	
Hypertension	0.733 (0.317, 1.694)
Diabetes mellitus	0.531 (0.161, 1.756)
Hyperlipidemia	0.699 (0.212, 2.302)
Asthma	2.004 (0.752, 5.340)
Laboratory tests	
ALT, per U/L	1.000 (0.996, 1.004)
AST, per U/L	0.999 (0.995, 1.002)
Creatinine, per mg/dL	0.791 (0.422, 1.484)

*The widths of confidence intervals have not been adjusted for multiplicity and cannot be used to infer a definitive presence of associations with outcome.

Table S2. Baseline predictors of mortality

Variable	Hazard Ratio (95% CI*)
Age, per year	1.168 (1.033, 1.321)
<70 years	--
≥70 years	11.335 (1.364, 94.172)
Female sex	0.571 (0.069, 4.759)
Region of enrollment	
United States	--
Non-United States	0.796 (0.178, 3.568)
Oxygen support status	
Noninvasive oxygen support	--
Invasive ventilation	2.783 (0.334, 23.187)
Duration of symptoms prior to remdesivir treatment, per day	1.019 (0.836, 1.241)
Comorbidities†	
Diabetes mellitus	2.048 (0.397, 10.567)
Hyperlipidemia	1.283 (0.154, 10.669)
Asthma	1.544 (0.183, 13.043)
Laboratory tests	
ALT, per U/L	1.003 (0.999, 1.008)
AST, per U/L	1.002 (1.000, 1.004)
Creatinine, per mg/dL	1.910 (1.221, 2.988)

*The widths of confidence intervals have not been adjusted for multiplicity and cannot be used to infer a definitive presence of associations with outcome.
†Hypertension excluded as no deaths were observed in patients with hypertension.

Figure S1. Patient Disposition

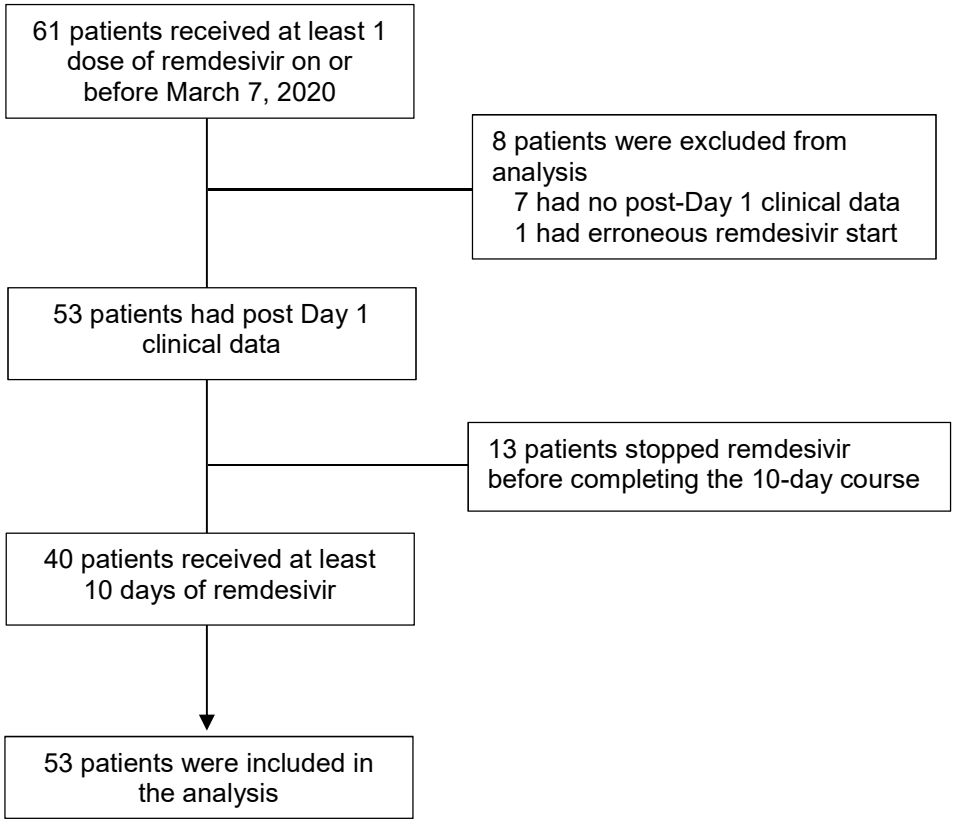
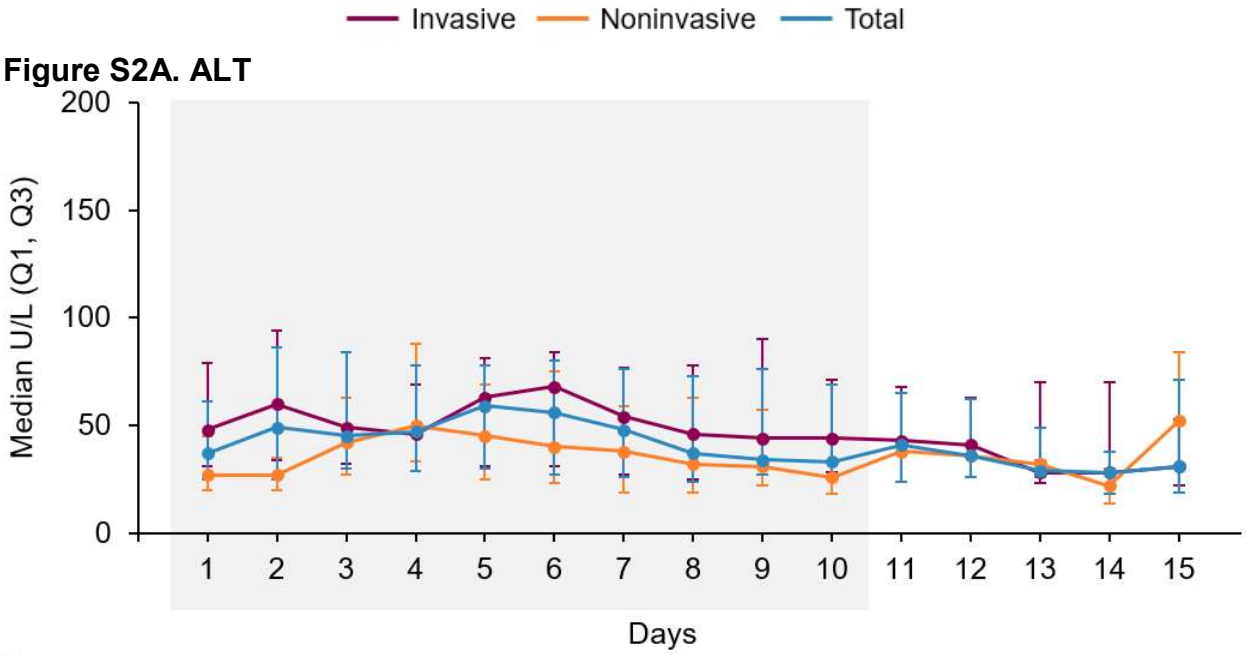
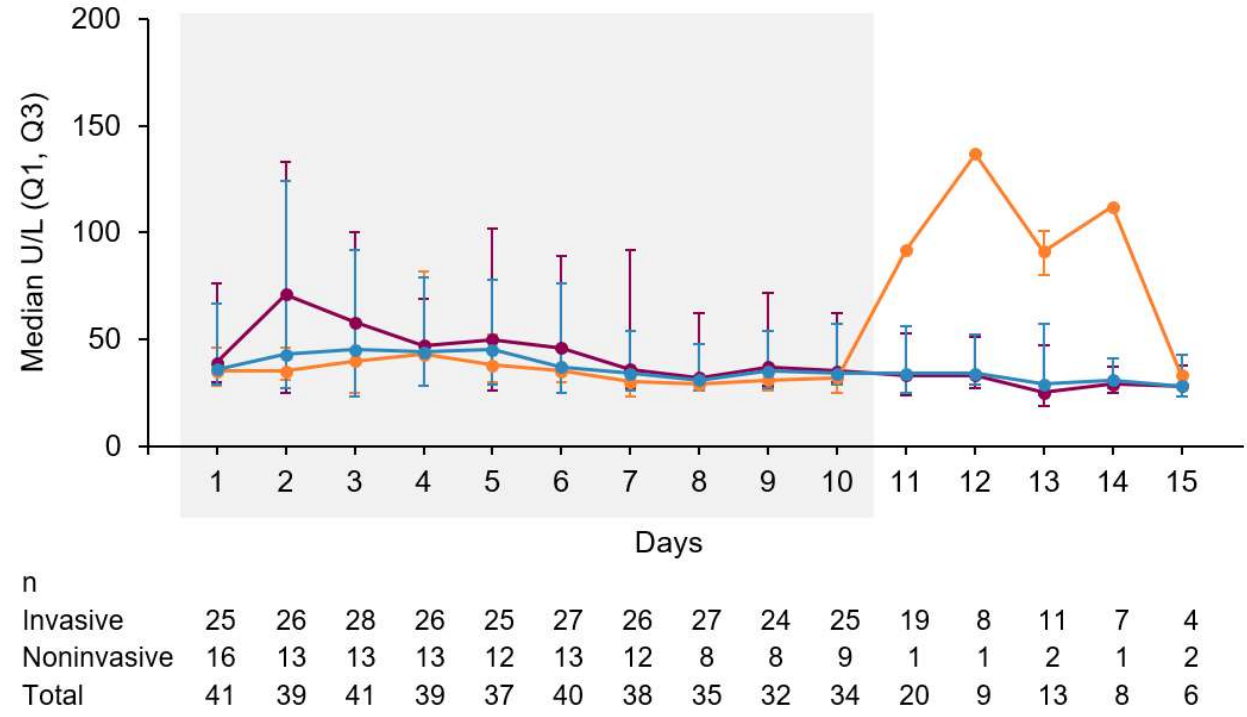


Figure S2. Changes in Serum ALT, AST, and Creatinine



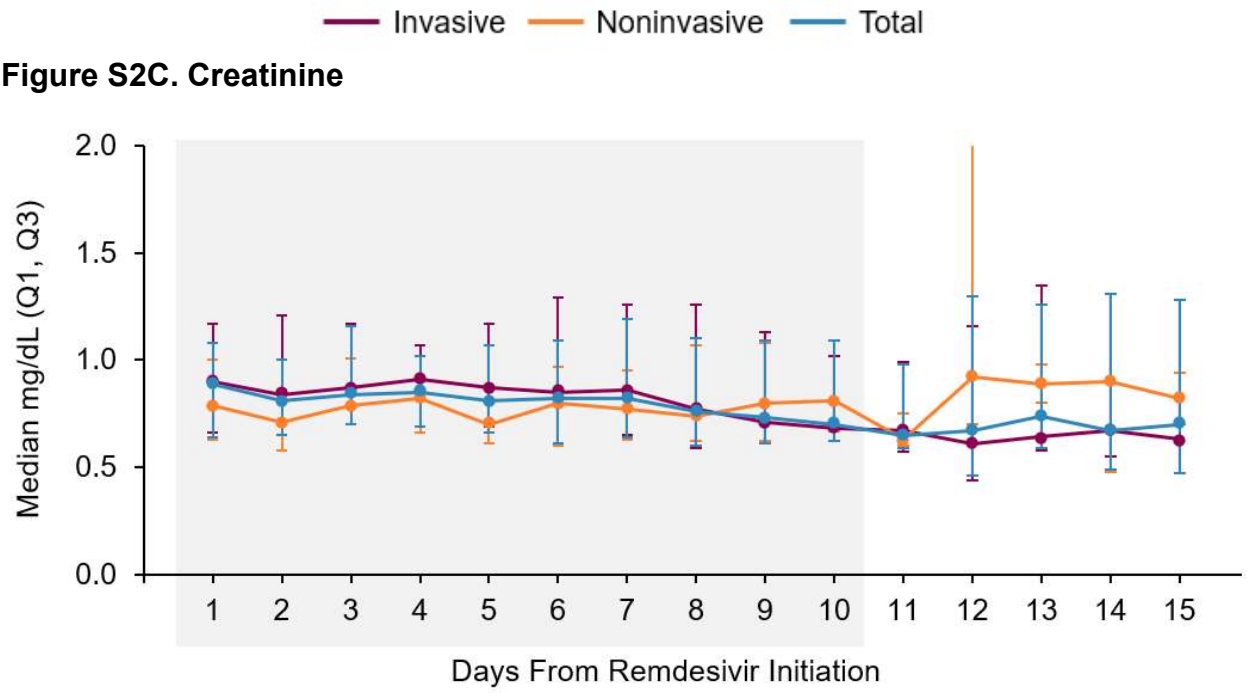
n															
Invasive	27	26	29	28	25	28	26	26	23	25	19	8	11	7	4
Noninvasive	16	13	14	13	12	13	12	8	9	9	1	1	2	2	2
Total	43	39	43	41	37	41	38	34	32	34	20	9	13	9	6



n															
Invasive	25	26	28	26	25	27	26	27	24	25	19	8	11	7	4
Noninvasive	16	13	13	13	12	13	12	8	8	9	1	1	2	1	2
Total	41	39	41	39	37	40	38	35	32	34	20	9	13	8	6

Shaded area indicates period of remdesivir treatment.

Figure S2. Changes in Serum ALT, AST, and Creatinine (continued)



n															
Invasive	30	29	31	30	28	31	31	30	27	25	20	12	14	12	5
Noninvasive	18	16	16	16	14	15	13	12	12	10	3	3	2	2	2
Total	48	45	47	46	42	46	44	42	39	35	23	15	16	14	7

Shaded area indicates period of remdesivir treatment.

Narratives of Deaths

A 79-year-old male in France with a medical history of hypothyroidism presented for care on January 22 (he reported onset of symptoms earlier that day). He was admitted to the hospital on January 25. His condition worsened, and he required invasive mechanical ventilation beginning on January 27. He received his first dose of remdesivir on January 29. A total of 8 doses were administered. The course was not completed due to acute kidney injury. Adverse events reported during treatment included acute renal failure requiring hemodialysis, thrombocytopenia, anemia, and respiratory superinfections including *Acinetobacter baumannii* and *Aspergillus fumigatus*. His condition deteriorated, and he died on February 14. The reported cause of death was septic shock.

A 68-year-old female with a medical history of diabetes, anemia, bipolar disorder, hypothyroidism, hyperlipidemia, and allergic rhinitis reported onset of symptoms on February 13 and was admitted to the hospital on February 22. Her condition worsened, and she required invasive mechanical ventilation beginning on February 29. She received her first dose of remdesivir on March 1 and received a total of 8 doses. The course was not completed due to liver function test elevation, which the investigator felt was caused by multiorgan system failure. Reported adverse events during treatment included acute kidney injury requiring continuous renal replacement therapy, hypotension, bradycardia, hepatitis, and transaminases increased. Her condition deteriorated, and she died on March 9. The reported cause of death was coronavirus infection.

A 75-year-old man in Italy with medical history of myasthenia gravis and prostatic hyperplasia reported onset of symptoms on February 16 and was admitted to the hospital on February 28. His

condition worsened, and he required noninvasive positive pressure ventilation (he did not receive invasive mechanical ventilation). He received his first dose of remdesivir on May 5. A total of 10 doses were administered. No additional adverse events were reported by the investigator during treatment. His condition deteriorated, and he died on March 15. The reported cause of death was respiratory distress.

A 72-year-old man with medical history of gastrointestinal cancer and diabetes reported onset of symptoms on February 23 and was admitted to the hospital on February 28. His condition worsened, and he required invasive mechanical ventilation beginning on March 7. He received his first dose of remdesivir on March 7. A total of 10 doses were administered. No additional adverse events were reported by the investigator during treatment. His condition deteriorated, and he died on March 21. The reported cause of death was multiorgan failure.

A 78-year-old man in Italy with no reported past medical history reported onset of symptoms on February 23 and was admitted to the hospital on February 28. His condition worsened, and he required invasive mechanical ventilation beginning on February 28. He received his first dose of remdesivir on March 7. A total of 6 doses were administered. The course was not completed due to the development of multiorgan system failure. His condition deteriorated, and he died on March 13. The reported cause of death was multiple organ failure.

A 72-year-old man in the United States with no significant past medical history reported onset of symptoms on February 22 and was admitted to the hospital on February 29. His condition worsened, and he required invasive mechanical ventilation beginning on March 3. He received his first dose of remdesivir on March 3. A total of 10 doses were administered. His condition

deteriorated, and he died on March 20. The reported cause of death was respiratory failure from acute respiratory distress syndrome.

A 77-year-old man in the United States with medical history that included asthma reported onset of symptoms on February 27 and was admitted to the hospital the same day. His condition worsened, and he required invasive mechanical ventilation beginning on March 6. He received his first dose of remdesivir on March 6, and a total of 10 doses were administered. His condition deteriorated, and he died on March 20. The reported cause of death was acute respiratory distress syndrome and multiorgan system failure due to Covid-19.